Engineering microscale cellular niches for three-dimensional multicellular co-cultures.

Journal: Lab Chip

Publication Year: 2009

Authors: Carlos P Huang, Jente Lu, Hyeryung Seon, Abraham P Lee, Lisa A Flanagan, Ho-Young Kim, Andrew J Putnam, Noo Li Jeon

PubMed link: 19495458

Public Summary:

Scientific Abstract:
Modeling the in vivo microenvironment typically involves placing cells in a three-dimensional (3D) extracellular matrix (ECM) in physiologically relevant context with respect to other cells. The mechanical and chemical features of 3D microenvironments play important roles in tissue engineering, tumor growth and metastasis, and in defining stem cell niches, and it is increasingly recognized that cells behave much differently when surrounded by a 3D ECM than when anchored to a 2D substrate. To create microenvironments that more closely mimic in vivo settings, here we describe a novel microfluidic device that allows multiple discrete constructs of 3D cell-laden hydrogels to be patterned in a sequence of simple steps. The microfluidic platform allows for real-time imaging of the interactions between multiple cell types exposed to both autocrine and paracrine signaling molecules, all within a 3D ECM environment. Detailed modeling determined that surface tension, hydrophobic interactions, and spatial geometry were important factors in containing the gels within distinct separate channels during the filling process. This allowed us to pattern multiple gel types side-by-side and pattern 3D gels spatially with tight dimensional control. Cells embedded in gels could be patterned by culturing MDA-MB-231 metastatic breast cancer cells and RAW 264.1 macrophage cells within distinct collagen type I and Matrigel ECM environments, respectively. Over a 7 day culture experiment, RAW cells invaded into neighboring gels containing MDA-MB-231 cells, but not into gels lacking cells. These studies demonstrate the versatility and potential of this new microfluidic platform to engineer 3D microscale architectures to investigate cell-cell and cell-matrix interactions.